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Dockets Management Branch
5600 Fishers Lane
Rockville, Maryland 20857
Rm. 4-62
(HFA-305)

DEPARTMENT OF HEALTH AND HUMAN SERVICES

FOOD AND DRUG ADMINISTRATION

[DOCKET NO. 81P-0306]

DUPLICATE OF THE ORIGINAL

SCHMID LABORATORIES, INC.; CONDOM WITH SPERMICIDAL LUBRICANT; PANEL RECOMMENDATION ON PETITION FOR RECLASSIFICATION

47FR18670
4-30-82

6-1-82

AGENCY: Food and Drug Administration.

ACTION: Notice.

SUMMARY: The Food and Drug Administration (FDA) is issuing for public comment the recommendation of the Obstetrics-Gynecology Device Section (the Section) of the Obstetrics-Gynecology and Radiologic Devices Panel that a condom with the spermicide nonoxynol-9 and the lubricant polyethylene glycol-400 (PEG-400) i.e, spermicidal lubricant, be reclassified from class III (premarket approval) into class II (performance standards). This recommendation was made after a review by the Section of a reclassification petition filed by Schmid Laboratories, Inc., Little Falls, NJ 07424. After reviewing the Section recommendation and any public comments received, FDA will approve or deny the reclassification petition by order in the form of a letter to the petitioner. FDA's decision on this reclassification petition will be announced in the FEDERAL REGISTER.

DATE: Comments by (insert date 30 days after date of publication in the FEDERAL REGISTER).

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ADDRESS: Written comments to the Dockets Management Branch (HFA-305), Food and Drug Administration, Rm. 4-62, 5600 Fishers Lane, Rockville, MD 20857.

FOR FURTHER INFORMATION CONTACT:

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SUPPLEMENTARY INFORMATION: On March 23, 1978 and October 21, 1980, Schmid Laboratories, Inc. (Schmid), Little Falls, NJ 07424, submitted to FDA premarket notifications under section 510(k) of the Federal Food, Drug, and Cosmetic Act (the act) (21 U.S.C. 360(k)) stating that it intended to market a device the manufacturer called "Prophylactic (Condom) with Contraceptive Lubricant" and "Condom with Spermicidal Lubricant (nonoxynol-9)." After reviewing the information in the premarket notifications, FDA determined that the device is not substantially equivalent to any device that was in commercial distribution before May 28, 1976, nor is the device substantially equivalent to a device that has been placed in commercial distribution since that date and subsequently reclassified. Accordingly, the new device is automatically classified into class III under section 513(f)(1) of the act (21 U.S.C. 360c(f)(1)).

Under section 515(a)(2) of the act (21 U.S.C. 360e(a)(2)), before a device that is in class III can be marketed, it must either be reclassified under section 513(f)(2) of the act or have an approved application for premarket approval under section 515 of the act. Such a device may be shipped in commerce, however, if there is in effect for the device an investigational device exemption under section 520(g) of the act (21 U.S.C. 360j(g)). There is no approved premarket approval application in effect for the "Prophylactic (Condom) with Contraceptive Lubricant" or the "Condom with Spermicidal Lubricant (nonoxynol-9)," and neither device is the subject of an investigational device exemption.

On February 2, 1979 and August 28, 1981, Schmid submitted to FDA reclassification petitions for the device under section 513(f)(2) of the act (Ref. 1). FDA referred the 1979 reclassification petition to the Obstetrics-Gynecology Section of the Obstetrics-Gynecology and Radiologic Devices Panel for review and recommendation. On May 14, 1979, the Section reviewed the petition and recommended that the device not be reclassified unless the labeling was changed.

FDA's action on the 1979 petition was delayed because of the need to determine how to regulate the product and what additional steps needed to be completed before it could be marketed. On May 1, 1981, FDA determined that the product should be regulated as a class III device. Because it believed that the 1979 petition did not provide evidence to demonstrate that performance standards are adequate to assure the safety and

effectiveness of a condom lubricated with a spermicide, FDA also determined that Schmid must demonstrate the contribution of nonoxynol-9 to the effectiveness of the device through data from adequate and well-controlled studies which compare the safety and effectiveness of the condom with nonoxynol-9 to a condom without a spermicide component (Ref. 2).

Following FDA's determinations, Schmid submitted its petition for reclassification of the "Condom with Spermicidal Lubricant (nonoxynol-9)" that is the subject of this notice. In this petition, the manufacturer's proposed labeling for the device stated that while scientific tests "strongly suggest that the addition of a spermicidal preparation to the lubricant enhances the overall contraceptive effectiveness of the condom, evidence of added contraceptive protection has not yet been established." Thereafter, FDA referred the 1981 petition to the Section for review and recommendation. On September 28, 1981, the Section reviewed the petition and recommended that FDA reclassify the device into class II provided the labeling bears a specific contraceptive effectiveness cautionary provision. This provision states:

> The condom with spermicidal lubricant is a contraceptive which combines a latex condom and a lubricant containing nonoxynol-9, a spermicide. Evidence of added contraceptive effectiveness has not been established with the addition of a spermicidal preparation to the condom.

To determine the proper classification of the device, the Section considered the criteria specified in section 513(a)(1) of the act. For the purpose of classification, the Section assigned to this generic type of device the name "condom with spermicidal lubricant" and identified this type of device as a latex rubber sheath with a lubricant that contains a spermicidal agent. The lubricant is on both the inner and outer surfaces of the sheath. The sheath covers the penis with a closely fitting membrane and is used for contraception and for prevention of transmission of venereal disease.

SUMMARY OF REASONS FOR RECOMMENDATION

The Section gave the following reasons in support of its recommendations on reclassification:

1. The device is not an implant, is neither life-sustaining nor life-supporting, and does not present a potential unreasonable risk of illness or injury.

2. Although general controls alone are insufficient to provide reasonable assurance of the safety and effectiveness of the device, sufficient scientific and medical data exist to establish a performance standard to provide such assurance.

3. The device is in physical contact with the body by means of contact with the penis and vagina; therefore, the material should meet a biocompatibility standard to prevent an adverse tissue reaction.

SUMMARY OF DATA ON WHICH THE RECOMMENDATION IS BASED

The Section stated that the safety and effectiveness of the condom with as a lubricant is well established (Ref. 3). The Section also reviewed the report of the Advisory Review Panel on OTC Contraceptives and Other Vaginal Drug Products (the Panel) (45 FR 82014; Dec. 12, 1980) in which the Panel concluded that nonoxynol-9 is generally recognized as safe and effective for over-the-counter (OTC) use as a vaginal contraceptive under the dosage conditions specified in the report (45 FR 82028).

Schmid conducted an in vitro study to determine the effectiveness of the condom with a lubricant with nonoxynol-9. Thirty healthy men, ranging from 19 to 46 years of age, were used as study subjects. Their semen characteristics, i.e., volume, pH, viscosity, sperm count, morphology and motility, were evaluated as normal. Observations of sperm motility in test and control condoms were made at 30, 60, and 120 seconds and 20 minutes post-ejaculation. The sperm motility in condoms with nonoxynol-9 in the lubricant was reduced from 60 percent to 10 percent within 30 seconds. The sperm motility in condoms without nonoxynol-9 in the lubricant remained above 50 percent. During this study, Schmid observed that there was no evidence of skin irritation on penises. Schmid referred to 54 citations related to animal and human studies on the safety and effectiveness of nonoxynol-9. Schmid also conducted the following preclinical tests for this device: the American Society for Testing and Materials (ASTM) standard tests for tensile strength and elongation, and the rabbit test for vaginal and penile irritation (Ref. 1).

The Section stated that the in vitro studies did not provide conclusive evidence that the addition of a spermicidal lubricant to the condom increases contraceptive effectiveness for the device. Nevertheless, the Section acknowledged that the device may provide added effectiveness over the condom without spermicidal lubricant. The Section concluded that to support its proposed claim of additional contraceptive effectiveness for the condom with spermicidal lubricant, the manufacturer must submit clinical data.

RISKS TO HEALTH

The Section noted that the condom with spermicidal lubricant, as well as any other condom, may present a risk of allergic reaction. Additionally, if the device were to fail, the risk of unwanted pregnancy or contraction of venereal disease is not less than with the use of a condom without spermicidal lubricant. The Section noted that these risks to health could be reduced by developing a performance standard addressing the materials, biocompatibility, and other characteristics of the device.

FDA notes in addition that a recent journal article raises questions about the possible teratogenic effects of nonoxynol-9 and other compounds used in vaginal spermicides (Ref. 4). The agency will address this issue when it issues a tentative final monograph on OTC contraceptives and other vaginal drug products. FDA believes, however, that any increase in exposure to nonoxynol-9 that would occur if the condom with spermicidal lubricant is reclassified and marketed would not present any significant safety risk.

ADDITIONAL FINDINGS

The Section recommended that the condom with spermicidal lubricant be reclassified into class II (performance standards) provided the device labeling includes the statement set forth above. The Section also recommended that the development of the standard be a low priority. Priority was recommended in accordance with the relative medical significance of this device in relation to other devices.

The Section believes that the labeling statement should be included under the "Description" section in the product label and should serve as the "statement of identity" under 21 CFR 801.61 to be included on the principal display panel of the device.

Therefore, whether the device is sold individually or a number of the devices are packaged and sold as a unit, all labeling would display the proposed statement. The Section explained that the use of a condom with spermicidal lubricant should not be a substitute for the use of a condom in conjunction with a vaginal spermicidal preparation.

The Section also recommended that the device labeling include an expiration date and proper instructions for use.

AGENCY'S COMMENT

The effectiveness of contraceptives is directly related to the method of contraception (e.g., condoms, spermicide) and to correct use. "Method-Effectiveness" describes effectiveness attained by users who follow manufacturers' instructions exactly and use the device each time during sexual intercourse. For example, of 100 women whose partners use condoms for 1 year, 3 women will become pregnant. Of 100 women who use spermicidal foams, jellies, and creams for 1 year, 2 to 3 women will become pregnant. "Use-Effectiveness" describes that level of effectiveness which is attained by typical users including those who either fail to use the product correctly or do not use it each time during sexual intercourse. The use-effectiveness of condoms ranges from 64 to 97 percent, that is, of 100 women whose partners incorrectly use condoms for 1 year, 3 to 36 women will become pregnant. The use-effectiveness of spermicidal foams, jellies, and creams range from 64 to 98 percent, that is, of 100 women who use these products for 1 year, 2 to 36 women will

become pregnant. The use of both a condom and a vaginal spermicidal preparation increases the probability of contraception in comparison to the use of a condom or a vaginal spermicidal preparation alone.

Currently marketed condoms without spermicidal lubricant are classified into class II (performance standards) (21 CFR 884.5300). The addition of a spermicidal lubricant to a condom does not detract from the use-effectiveness of a condom without spermicidal lubricant. Moreover, the in vitro data submitted by Schmid suggest that the condom with spermicidal lubricant may provide an increase in use-effectiveness in any case where the condom is used incorrectly, is defective, slips off during or after intercourse, or ruptures during intercourse. Although Schmid did not submit clinical data to support its claim of additional contraceptive effectiveness for the condom with spermicidal lubricant, FDA believes that the device might provide an increase in use-effectiveness and recognizes that clinical studies of the device would be difficult to conduct and may not produce evidence justifying the effort of collecting it. FDA has therefore tentatively concluded that its previous position should be modified and that the evidence of added effectiveness that clinical studies might produce should not be required, and that reclassification into class II would provide reasonable assurance of the device's effectiveness.

FDA believes that the labeling statement recommended by the Section cannot provide a basis for reclassification because, under section 513(a)(3) of the act (21 U.S.C. 360c(a)(3)) and § 860.134 of the regulations governing reclassification (21 CFR 860.134), a device may not be reclassified absent a showing, by valid scientific evidence, that the reclassification requested will provide reasonable assurance of the effectiveness, as well as the safety, of the device. The Section's recommended labeling statement asserts that no evidence of added contraceptive effectiveness has been established with the addition of a spermicidal preparation to the condom, a statement that may be interpreted as undermining the required finding of reasonable assurance of effectiveness. In addition, FDA traditionally has regarded such disclaimers as misbranding products. See, e.g., United States v. Nutrition Service, Inc., 227 F. Supp. 375 (W.D. Pa. 1964), aff'd. 347 F.2d 233 (7th Cir. 1965); United States v. Millipax, Inc., 313 F.2d 152 (7th Cir.), Cert. denied, 373 U.S. 903 (1963); United States v. An Article of Drug * * * Jenasol, 320 F. 2d 564 (3d Cir.) cert. denied sub nom., Schere v. United States, 375 U.S. 953 (1953). FDA believes, however, that the following modification of the Section's proposed labeling is both lawful and appropriate:

> The presence of a spermicide in this product may be helpful in decreasing the risk of pregnancy should the condom fail or be misused.

FDA invites comments on these tentative conclusions and the Section's recommendation that this condom with spermicidal lubricant be reclassified from class III into class II provided the labeling bears the contraceptive effectiveness cautionary statement set out above.

REFERENCES

The transcripts of the Section meeting and the following material are on public file in the Dockets Management Branch (address above) where they may be seen by interested persons between 9 a.m. and 4 p.m., Monday through Friday.

1. "Prophylactic (Condom) with Contraceptive Lubricant," Petition for Reclassification, Schmid Laboratories, Inc., February 1979, Docket No. 80P-0075; "Condom with Spermicidal Lubricant (nonoxynol-9)," Petition for Reclassification, Schmid Laboratories, Inc., August 1981, Docket No. 81P-0306.

2. Letter, Mark Novitch, M.D., Acting Commissioner of Food and Drugs, to William R. Pendergast, May 1, 1981.

3. "Barrier Methods," Population Reports, Series H, No. 2, The George Washington University Medical Center, Washington, DC, 1974.

4. Jick, et al., "Vaginal Spermicides and Congenital Disorders," Journal of the American Medical Association, 245:1329-1332, 1981.

After considering the economic consequences of approving this reclassification petition, FDA certifies that this notice requires neither a regulatory impact analysis, as specified in Executive Order 12291, nor a regulatory flexibility analysis, as defined in the Regulatory Flexibility Act (Pub. L. 96-354). If FDA approves the petition, the petitioner and any other future manufacturer of the device would be relieved of the costs of complying with the premarket approval requirements in section 515 of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 360e). The costs the petitioner would incur from reclassification into class II cannot be quantified until performance standards are developed. Because of statutory deadlines (section 513(f)(2) of the act) and requirements in the regulations (21 CFR 860.134(b)(5)), FDA is required to publish this notice in the FEDERAL REGISTER as soon as practicable. As authorized by section 8(a)(2) of Executive Order 12291, FDA is publishing in the FEDERAL REGISTER this notice without clearance of the Director, Office of Management and Budget. As soon as practicable, FDA will notify that office of the publication of this notice.

Interested persons may, on or before (insert date 30 days after date of publication in the FEDERAL REGISTER), submit to the Dockets Management Branch (address above), written comments on this recommendation. Two copies of any comments are to be submitted, except that individuals may submit one copy. Comments are to be identified with the generic name of the device and the docket number found in brackets in the heading of this document. Received comments may be seen in the office above between 9 a.m. and 4 p.m., Monday through Friday.

Dated: April 26, 1982.

APR 26 1982

Joseph P. Hile
Associate Commissioner for
Regulatory Affairs

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Marcia Finlayson